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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER
YAEN, CHRISTOPHER H

ART UNIT	PAPER NUMBER
1642	15

DATE MAILED: 07/30/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/006,069	REBAR ET AL.	
	Examiner	Art Unit	
	Christopher H Yaen	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 May 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-98* is/are pending in the application.

4a) Of the above claim(s) *1-20,23,25-85 and 90-98* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *21,22,24 and 86-89* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 7, 8, 12, 13
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Election/Restrictions

1. Applicant's election without traverse of group III in Paper No. 14 is acknowledged. Applicant election with traverse of a VOP 32-E nucleic acid in Paper No. 14 is acknowledged. The traversal is on the grounds that the election requirement was improper. This was not found persuasive because there are multiple sequence found in tables 3 and 4 which would require searching multiple permutations with each zinc finger protein claimed. A search for all the target sequences with each zinc finger protein listed in tables 3 and 4 would require an undue search. As such, applicant's election of VOP 32-E limits the search to a single zinc finger protein with a single target sequence allowing for the best search of prior art.

2. The requirement is still deemed proper and is therefore made FINAL.

3. Claims 1-98 are pending, claims 1-20, 23, 25-85, and 90-98 are withdrawn from further consideration as being drawn to a non-elected invention. Claim 23 is withdrawn from further consideration because the claim is drawn to proteins that contain 6 zinc finger motifs, the elected sequence or protein (VOP 32-E) is a protein that consists of three zinc finger motif.

4. Therefore, claims 21-22, 24, and 86-89 are examined on the merits.

Information Disclosure Statement

5. The Information Disclosure Statements filed 4/8/02, 3/25/02, 10/21/02, 1/21/03 (paper nos. 7,8,12, and 13) are acknowledged and considered. A signed copy of the IDS is attached hereto.

Claim Objections

6. Claims 21-22,24,86-89 are objected to because of the following informalities: the claims read on non-elected groups. Appropriate correction is required.

Claim Rejections - 35 USC § 101

7. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

8. Claims 21-22, and 24 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. The claims, as written, do not sufficiently distinguish over nucleic acids as they exist naturally because the claims do not particularly point out any non-naturally occurring differences between the claimed products and the naturally occurring products. In the absence of the hand of man, the naturally occurring products are considered non-statutory subject matter. *See Diamond v. Chakrabarty*, 447 U.S. 303, 206 USPQ 193 (1980). The claims should be amended to indicate the hand of the inventor, e.g., by insertion of "Isolated" or "Purified" as taught by page 73 of specification, for example. See MPEP 2105.

Claim Rejections - 35 USC § 112, 1st paragraph

9. Claims 86-89 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a composition comprising a nucleic acid encoding a polypeptide that comprises a zinc finger for in vitro use, does not reasonably provide enablement for a pharmaceutical composition comprising a nucleic acid encoding a polypeptide that comprises a zinc finger protein. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

Claims 86-89 are broadly drawn to "pharmaceutical compositions" comprising a nucleic acid molecules encoding a polypeptide that comprises a zinc finger protein.

The specification teaches the identification of zinc finger proteins that are able to bind the VEGF. The specification further contemplates the use of the nucleic acid molecule encoding the zinc finger proteins for the modulation of angiogenesis, wherein the administration of the zinc finger proteins would regulate blood vessel formation and thereby potentially treat diseases associated with blood vessel formation such as cancer (page 7, lines 14+).

However, one cannot extrapolate the teachings of the specification to the scope of the claims because the specification provides no exemplification of or guidance on how to use the claimed pharmacuetical (i.e. retroviral vaccine) for immunization or therapeutic purposes with any predictability. With regards to tumor immunotherapy, the goal of tumor vaccination is the induction of tumor immunity to prevent tumor recurrence and to eliminate residual disease. However, gene therapy against tumors is highly

unpredictable as underscored by Crystal, R.G. (Science, Vol. 270, October 1995, pages 404-410) who teaches that in tumor vaccine studies intended to evoke a tumor-directed immune response, there is no convicining evidence (other than anecdotal case reports) that tumors actually regress, despite the promising observations in experimental animals. In other words, humans are not simply large mice (page 409, 1st column). More recently, Tait *et al.* (Clin.Canc.Res., Vol. 5, July 1999, pages 1708-1714) revealed just how unpredictable gene therapy was in the clinical setting. The authors' prior phase I trial of 12 patients with extensive ovarian cancer treated with a retroviral vector expressing the BRCA1 splice variant (LXSN-BRCA1sv) demonsrated vector stability, minimal immune response, gene transfer and expression, and some tumor reduction in the patients (page 1708, 2nd column, 2nd paragraph). In contrast, the Phase II trial inititiated in pateints with stage III and IV grade ovarian cancer, showed a high preponderance for vector instability (vector was degraded rapidly), a rapid immunological response invoking neutralizing antibodies to the retroviral vector, and no clinical response to the therapy. Although the difference in response to the therapy may be attributed to differences in immunocompetence between the phase I and II patients (page 1712, 2nd column), the end result seems to indicate that further experimentation is necessary prior to the successful application of DNA vaccines, especially with the regards to cancer therapy. Further, treatment of cancer in general is at most unpredictable, as underscored by Gura (Science, v278, 1997, pp.1041-1042) who discusses the potential shortcomings of potential anti-cancer agents including extrapolating from in-vitro to in-vivo protocols, the problems of drug testing in knockout

mice, and problems associated with clonogenic assays. Indeed, since formal screening began in 1955, thousands of drugs have shown activity in either cell or animal models, but only 39 that are used exclusively for chemotherapy, as opposed to supportive care, have won approval from the FDA (page 1041, 1st column) wherein the fundamental problem in drug discovery for cancer is that the model systems are not predictive. All of this underscores the criticality of providing workable examples which is not disclosed in the specification, particularly in an unpredictable art, such as cancer therapy.

In view of the teachings above, and the lack of guidance and or exemplification in the specification, it would not be predictable for of skill in the art to use the pharmaceutical compositions as contemplated in the disclosure. Thus, it would require undue experimentation by one of skill in the art to practice the invention as claimed.

Claim Rejections - 35 USC § 102

10. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

11. Claims 21 and 24 are rejected under 35 U.S.C. 102(b) as being anticipated by Choo *et al* (US Patent 6,007,988, IDS AG). Claims are drawn to a nucleic acid molecule encoding a zinc finger polypeptide that binds to a target site comprising a nucleotide sequence as specified in Table 3. The claims are further limited to a fusion

protein with regulatory domains. Choo *et al* disclose a library of zinc finger binding motifs that bind to specific binding targets. Choo *et al* further disclose of fusing the zinc finger protein to a regulatory domains in the context of selecting a protein with an antibiotic. Furthermore, Choo *et al* teach that the protein can be inserted into viral vectors (adeno) for use in in vitro expression or in vivo expression. Although the reference does not characterize that the nucleic acid encodes a protein that binds to the target sequence of table 3, the claims are drawn to the product *per se* and inherently, such a nucleic acid would encode a polypeptide that would bind the target sequence listed in table 3. Further, the specification teaches zinc finger proteins can include a variety of different component fingers of different amino acid sequence provided that the zinc fingers bind to the same target (see page 35). Thus, the claimed nucleic acid encodes a protein that appears to be the same as the prior art.

12. Claim 21 is rejected under 35 U.S.C. 102(b) as being anticipated by Feldmann H *et al* (P38082 EMBL/GenBank/DDBJ database, submitted 1994). See above for claim limitations. Feldmann H *et al* taught a nucleic acid encoding a protein sequence that is a zinc finger protein. This sequence was publicly available before the time of filing. Although the reference does not specifically teach that the nucleic acid encodes a protein that binds to the target sequence of table 3, the claims are drawn to the product *per se* and inherently, such a nucleic acid would encode a polypeptide would bind the target sequence listed in table 3. Thus, the claimed nucleic acid encodes a protein that appears to be the same as the prior art. The office does not have the facilities and resources to provide the factual evidence needed in order to establish that the product

of the prior art does not possess the same material, structural and functional characteristics of the claimed product. In the absence of evidence to the contrary, the burden is on the applicant to prove that the claimed product is different from those taught by the prior art and to establish patentable differences. See In re Best 562F.2d 1252, 195 USPQ 430 (CCPA 1977) and Ex parte Gray 10 USPQ 2d 1922 (PTO Bd. Pat. App. & Int. 1989).

13. Claims 21,24, and 86-89 rejected under 35 U.S.C. 102(b) as being anticipated by Barbas *et al* (US Patent 6,140,081, IDS AB). Se above for claim limitations. Barbas *et al* discloses the discovery of nucleic acid molecules encoding zinc finger proteins that bind to specific DNA targets and further teaches the use of said zinc finger proteins to modulate nucleotide function. Barbas *et al* also specifically teach that such nucleic acids can be in the form of a fusion protein that is operatively linked to "transcription modulating factors" (see column 4 lines 19-25), and that such nucleic acid molecules can be in the form of a pharmaceutical compositions (see column 13). It is further disclosed that the composition can be in the form of a retroviral vector for administration to a subject (see column 18). Although the reference does not specifically teach that the nucleic acid encodes a protein that binds to the target sequence of table 3, the claims are drawn to the product *per se* and inherently, such a nucleic acid would encode a polypeptide would bind the target sequence listed in table 3. Thus, the claimed nucleic acid encodes a protein that appears to be the same as the prior art. The office does not have the facilities and resources to provide the factual evidence needed in order to establish that the product of the prior art does not possess the same

material, structural and functional characteristics of the claimed product. In the absence of evidence to the contrary, the burden is on the applicant to prove that the claimed product is different from those taught by the prior art and to establish patentable differences. See In re Best 562F.2d 1252, 195 USPQ 430 (CCPA 1977) and Ex parte Gray 10 USPQ 2d 1922 (PTO Bd. Pat. App. & Int. 1989).

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christopher H Yaen whose telephone number is 703-305-3586. The examiner can normally be reached on Monday-Friday 9-5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa can be reached on 703-308-3995. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4242 for regular communications and 703-305-3014 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Christopher Yaen
Art Unit 1642
July 25, 2003

Gary B Nelson (PSA)